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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SKELDING, ZACHARY S	

ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/693,233	KAYMAKCALAN ET AL.	
	Examiner	Art Unit	
	ZACHARY SKELDING	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-17,21-24,31,34,35,42,43,45,48 and 52-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-17, 21-24, 31, 34, 35, 42, 43, 45, 48, and 52-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed June 4, 2008 has been entered.

   Claims 1-14, 18-20, 25-30, 32-33, 36-41, 44, 46-47, and 49-51 have been canceled.

   Claims 15, 17, 21, 23, 24, 31, 35, 36, 42, 43, 45, 48, 52, and 53 have been amended.

   Claims 54-56 are new.

   Claims 15-17, 21-24, 31, 34, 35, 42, 43, 45, 48, and 52-56 are pending.

   Claims 15-17, 21-24, 31, 34, 35, 42, 43, 45, 48, and 52-56 are under consideration as they read on a method for treating arthritis by administering an anti-TNFα antibody, wherein the species of arthritis is "rheumatoid arthritis".

2. The previous rejections of record can be found in the previous Office Action, mailed March 4, 2008.

   The previous rejection under 35 U.S.C. § 102(b) has been withdrawn in view of applicant's amendment to the claims.

   However, it should noted that applicant's argument on page 7, 2nd paragraph of their remarks is not found convincing primarily because applicant is arguing a limitation not claimed, i.e., a dose of 0.01 mg/kg whereas the claims recite a dose of 0.01 - 0.1 mg/kg.

   New Grounds of Rejection are put forth below.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

   > The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 15-17, 21-24, 31, 34, 35, 42, 43, 45, 48, 52 and 53 stand rejected, and newly added claims 54 and 55 are rejected, under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating arthritis with 0.1 mg/kg of any anti-TNFα antibody or for treating arthritis with 0.1 mg/kg of any anti-TNFα antibody wherein said arthritis is treated by alleviating the symptom vascularity or for treating arthritis with 0.1 mg/kg of the D2E7 anti-TNFα antibody or an anti-TNFα antibody having the properties recited in claim 1, wherein arthritis is treated by alleviating the symptoms from the group consisting of bone erosion, cartilage erosion and inflammation, *does not reasonably provide enablement for* treating arthritis with 0.01-0.1 mg/kg of any anti-TNFα antibody or for treating arthritis with 0.01-0.1 mg/kg of any anti-TNFα antibody wherein arthritis is

treated by alleviating the symptoms from the group consisting of bone erosion, cartilage erosion, inflammation, and vascularity or for treating arthritis with 0.1 mg/kg of the infliximab anti-TNFα antibody wherein arthritis is treated by alleviating the symptoms from the group consisting of bone erosion, cartilage erosion and inflammation or for the methods of claims 54 and 55 which comprising administering "an anti-TNFα drug", essentially for the reasons of record as put forth in the prior Office Action mailed March 4, 2008 and as put forth further below with respect to new claims 54 and 55.

With respect to the previously rejected claims, in support of the claimed method applicant continues to point to the disclosure of the instant specification using reasoning substantively the same as their previous remarks filed November 8, 2008.

Applicant's argument are not found convincing for the reasons of record put forth in the prior Office Action mailed March 4, 2008.

With respect to the new claims, the phrase administering "an anti-TNFα drug," given its broadest reasonable interpretation consistent with the instant specification, reads on for example, not only anti-TNFα antibodies but also on anti-TNFα drugs such as small-molecule TNFα binding drugs.

However, despite considerable incentives, viable leads for direct small-molecule inhibitors of TNF-α were not known in the art as of applicant's filing date (see, e.g., He et al., Science. 2005 Nov 11;310(5750):1022-5, in particular page 1022), demonstrating the considerable uncertainty associated with making such a molecule.

Thus, undue experimentation would be required to practice the claimed invention commensurate with the scope of the claims from the written disclosure alone. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 15-17, 21-24, 31, 34, 35, 42, 43, 45, 48, 52 and 53 stand rejected, and newly added claims 54-56 are rejected, under 35 U.S.C. § 103(a) as unpatentable over Stephens et al. (Antibody Therapeutics (1997), pp 317-340, eds. Harris et al., CRC: Boca Raton, Fla.), in view of Salfeld et al. (US Patent No. 6,258,562) and den Broeder et al. (Rheumatology

(Oxford). 2002 Jun;41(6):638-42), essentially for the reasons of record as put forth in the prior Office Action mailed March 4, 2008.

Applicant continues to argue in substantially the same way as in applicant's previous remarks filed November 8, 2008 that the instant claims are non-obvious over the cited references because the references allegedly fall short in their teachings as combined, teach away from the claimed invention, and motivation to combine the cited references is lacking.

Applicant's argument are not found convincing for the reasons of record put forth in the prior Office Action mailed March 4, 2008.

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

   A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

   Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 15-17, 21-24, 31, 34, 35, 42, 43, 45, 48, 52 and 53 stand rejected and newly added claims 54-56 are rejected, under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1–7, 17, 19, 20, 36-39, 49, 51, 52, 68, 69 and 70 of U.S. Patent No. 6,509,015 in view of Salfeld et al. (US Patent No. 6,258,562) and den Broeder (Rheumatology (Oxford). 2002 Jun;41(6):638-42), essentially for the reasons of record as put forth in the prior Office Action mailed March 4, 2008.

   Applicant continues to argue in substantially the same way as in applicant's previous remarks filed November 8, 2008 that the instant claims are non-obvious over the cited references,

primarily because they encompass applicant's allegedly unexpected discovery that low doses of anti-TNFα can treat rheumatoid arthritis.

Applicant's argument are not found convincing for the reasons of record put forth in the prior Office Action mailed March 4, 2008.

Thus, as put forth in detail in the previous Office Actions of March 4, 2008 the reference claims, in view of the teachings of Salfeld and den Broeder, render the claimed invention obvious.

9. Claims 15-17, 21-24, 31, 34, 35, 42, 43, 45, 48, 52 and 53 stand rejected and newly added claims 54-56 are rejected, under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 7,223,394 in view of Salfeld et al. (US Patent No. 6,258,562) and den Broeder (Rheumatology (Oxford). 2002 Jun;41(6):638-42), essentially for the reasons of record as put forth in the prior Office Action mailed March 4, 2008.

   Applicant continues to argue in substantially the same way as in applicant's previous remarks filed November 8, 2008 that the instant claims are non-obvious over the cited references, primarily because they encompass applicant's allegedly unexpected discovery that low doses of anti-TNFα can treat rheumatoid arthritis.

   Applicant's argument are not found convincing for the reasons of record put forth in the prior Office Action mailed March 4, 2008.

   Thus, as put forth in detail in the previous Office Actions of March 4, 2008, the reference claims, in view of the teachings of Salfeld and den Broeder, render the claimed invention obvious.

10. Claims 15-17, 21-24, 31, 34, 35, 42, 43, 45, 48, 52 and 53 stand rejected and newly added claims 54-56 are rejected, under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 17, 41, 79, 86, 103, 110, 115, 122, 127 and 134 of USSN 11/233,252 in view of Salfeld et al. (US Patent No. 6,258,562) and den Broeder (Rheumatology (Oxford). 2002 Jun;41(6):638-42), essentially for the reasons of record as put forth in the prior Office Action mailed March 4, 2008.

    Applicants further requests the Examiner hold in abeyance all obviousness-type double patenting rejections based on co-pending applications until allowable subject matter is indicated, at which point the Applicants will address this issue.

    Applicant's request is acknowledged, however, Applicant is advised that the instant rejection will be maintained until such time as a terminal disclaimer signed by the assignee and fully compliant with 37 CFR 3.73(b) is submitted.

Thus, as put forth in detail in the previous Office Actions of March 4, 2008, the reference claims, in view of the teachings of Salfeld and den Broeder, render the claimed invention obvious.

New Grounds of Rejection follow.

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

12. Claims 52-56 are rejected under 35 U.S.C. 102(a) as being anticipated by den Broeder (Rheumatology (Oxford). 2002 Jun;41(6):638-42) as evidenced by the instant specification at Figure 5 and the paragraph bridging pages 6-7.

Den Broeder teaches a dose titration clinical trial of the D2E7 anti-TNFα antibody in which rheumatoid arthritis patients were effectively treated with a doses of, e.g., 0.25 and 0.5 mg/kg/2-4 weeks (see, e.g., paragraph bridging pages 639-640 and page 640, right column, 1st paragraph).

Since den Broeder teaches treatment of the same disorder, i.e., rheumatoid arthritis, with the same antibody, i.e., D2E7, at doses encompassed by the instant claims, den Broeder inherently teaches a method of treating the arthritis symptoms recited in the instant claims using an antibody meeting the limitations of the instant claims as evidenced by the instant specification at Figure 5 and the paragraph bridging pages 6-7.

Thus, the instant claims are anticipated by den Broeder.

13. Claims 52, 53 and 56 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 52, 53 and 56 recite a method of treatment comprising administering an anti-TNFα drug "selected from the group consisting of…enantercept."

However, the word "enantercept" does not appear in the instant specification.

Thus instant claim recites a limitation not clearly disclosed in the specification as-filed, and changes the scope of the instant disclosure as-filed. Such a limitation recited in the instant claim, which did not appear in the specification as filed, introduces a new concept and

violates the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office action.

Alternatively, applicant is invited to provide sufficient written support for the limitation indicated above. See MPEP 714.02 and 2163.06.

14. No claim is allowed.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ZACHARY SKELDING whose telephone number is (571)272-9033. The examiner can normally be reached on Monday - Friday 8:00 a.m. - 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Zachary Skelding, Ph.D.
Patent Examiner
September 3, 2008

/Michail A Belyavskyi/

Primary Examiner, Art Unit 1644